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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09 731,457	12 06 2000	Ian Popoff	RTS-0182	1220

7590

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EXAMINER

SCHULTZ, JAMES

ART UNIT

PAPER NUMBER

1635

DATE MAILED: 03 28 2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

**Advisory Action**

Application No.

09/731,457

Applicant(s)

POPOFF ET AL.

Examiner

J. Douglas Schultz

Art Unit

1635

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 03 March 2003 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

**PERIOD FOR REPLY** [check either a) or b)]

- a) ☒ The period for reply expires 4 months from the mailing date of the final rejection.  
b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.  
ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☐ A Notice of Appeal was filed on \_\_\_\_\_. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.  
2. ☒ The proposed amendment(s) will not be entered because:  
(a) ☒ they raise new issues that would require further consideration and/or search (see NOTE below);  
(b) ☐ they raise the issue of new matter (see Note below);  
(c) ☒ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or  
(d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: See Continuation Sheet.

3. ☐ Applicant's reply has overcome the following rejection(s): \_\_\_\_\_.  
4. ☐ Newly proposed or amended claim(s) \_\_\_\_\_ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).  
5. ☒ The a) ☐ affidavit, b) ☐ exhibit, or c) ☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation Sheet.  
6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.  
7. ☒ For purposes of Appeal, the proposed amendment(s) a) ☒ will not be entered or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: \_\_\_\_\_

Claim(s) objected to: \_\_\_\_\_

Claim(s) rejected: 1, 2, 4-10, and 12-15, for reasons of record

Claim(s) withdrawn from consideration: \_\_\_\_\_

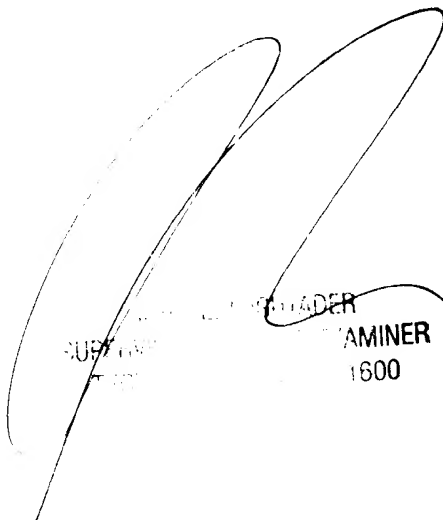
8. ☐ The proposed drawing correction filed on \_\_\_\_\_ is a) ☐ approved or b) ☐ disapproved by the Examiner.  
9. ☐ Note the attached Information Disclosure Statement(s) (PTO-1449) Paper No(s). \_\_\_\_\_.  
10. ☐ Other: \_\_\_\_\_

Continuation of 2. NOTE: Continuation of 2. NOTE: Claim 1 has been amended to recite oligonucleotides directed to specific and discrete regions of the target, such that the claim now encompasses distinct oligonucleotides that have not been explicitly examined heretofore. The proposed amendment will not be entered, since a search for each distinct oligonucleotide as newly recited would raise new prior art and/or new search issues not previously considered.

Continuation of 5. does NOT place the application in condition for allowance because the arguments newly raised by applicant are not considered convincing. Applicants allege that while the reference of Taylor et al. indicates that antisense can be generated against any transcript of known sequence, that Taylor does not indicate whether that sequence would actually have inhibitory activity. This is not convincing, because Taylor cites that with available software screening techniques and chimeras, that only 3-6 sequences need to be screened in order to find one that inhibits a transcript 66%-95%. One of ordinary skill in the art would therefore have a reasonable expectation using the teachings of the prior art in making oligos that inhibit the expression of applicants' claimed target.

Applicants also argue that Hayes et al. does not provide motivation to inhibit applicants' instant target, because Hayes et al. disclose only a role for the p48 subunit in regulating the activity of E2F1, and do not teach or suggest any role for the instantly contemplated p127 subunit of Damage-specific DNA binding protein 1 (DDB1) in such regulation. This is not convincing, because Hayes clearly teach that both subunits are required for optimal binding to the E2F1 (p. 243, bridging para. to 244, fig. 5). Moreover, co-transfection of both subunits is required to stimulate E2F1 transcription; importantly, transfection of any one subunit was not able to induce E2F1 transcription (p. 246, lines 5 and 6). Such results clearly indicate that targeting either subunit of DDB1 would be sufficient to interfere with E2F1-mediated transcription, and is contrary to Applicants' assertion that Hayes only provides motivation to target the p48 subunit. In summary, Hayes et al. provide motivation to target the instantly claimed p127 subunit of DDB1, because Hayes et al. teach that both subunits are required to stimulate E2F1-mediated transcription.

Applicants remaining arguments have been addressed in full in the previous Office action mailed November 1, 2002.

  
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